EXHIBIT 6

Executive Summary

Executive Summary of the Ovarian Cancer Evidence Review Conference

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The Centers for Disease Control and Prevention awarded funding to the American College of Obstetricians and Gynecologists to develop educational materials for clinicians on gynecologic cancers. The American College of Obstetricians and Gynecologists convened a panel of experts in evidence review from the Society for Academic Specialists in General Obstetrics and Gynecology and content experts from the Society of Gynecologic Oncology to review relevant literature, best practices, and existing practice guidelines as a first step toward developing evidence-based educational materials for women's health care clinicians about ovarian cancer. Panel members conducted structured literature reviews, which were then reviewed by other panel members and discussed at a virtual meeting of stakeholder professional and patient advocacy organizations in February 2022. This article is the executive summary of the relevant literature and existing recommendations to guide clinicians in the prevention, early diagnosis, and special considerations of ovarian cancer. Substantive knowledge gaps are noted and summarized to provide guidance for future research.

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The Centers for Disease Control and Prevention funded the American College of Obstetricians and Gynecologists (ACOG) to create and disseminate educational material for clinicians on the early diagnosis and prevention of gynecologic cancers and early-onset breast cancer.[1,2] Ovarian cancer is relatively rare, ranking 17th among all cancers in the United States, with an incidence of 10.6 per 100,000 from 2015 to 2019.[3,4] However, ovarian cancer is the fifth

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Rebecca Brooks is a member of an AstraZeneca speakers' bureau related to ovarian cancer, a past advisory board member for Tempus, a past advisory board member and consultant for GSK and Merck & Co., Inc., and a past non-branded speaker for Clinical Care Options, CURE Educated Patient Summit, and Med Educator Consortium. Julia Sage O'Hara is an employee of the American College of Obstetricians and Gynecologists. David Chelmow is the immediate past president of ASCCP and the Council of University Chairs of Obstetrics and Gynecology, receives a stipend as the editor-in-chief of the Medscape Obstetrics and Gynecology Clinical Reference Book, and was on the American Board of Obstetrics and Gynecology Board of Directors during the evidence review period. David Chelmow is a member of the U.S. Preventive Services Task Force (USPSTF). This article does not necessarily represent the views and policies of the USPSTF. All authors except for Julia Sage O'Hara received a one-time payment from ACOG for their participation in the development of ovarian cancer educational materials. The other authors did not report any potential conflicts of interest.

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most common cause of cancer death in women in the United States and is the deadliest form of gynecologic cancer.[5,6] Because of its high mortality rate, ovarian cancer was chosen as the second gynecologic cancer for educational material development. To ensure that these materials were based on the most current literature and guidelines, an extensive literature review was conducted. This article is the evidence summary, which is presented in detail in Appendices 2–8, available online at http://links.lww.com/AOG/D170. The health care professional educational material is available online at acog.org.

METHODS

Methods for the evidence review and educational material development closely followed the process for the early-onset breast cancer and uterine cancer projects.[1,2] The ACOG convened an expert panel to identify the best evidence and practices from the literature and existing relevant guidelines. The panel was recruited from the Society for Academic Specialists in General Obstetrics and Gynecology to review and summarize the evidence. The panel was supplemented by representatives from the Society of Gynecologic Oncology. Panel members were selected on the basis of expertise in evidence review and synthesis. The panel developed research questions and used the PICO criteria (P=patient, problem, or population; I=intervention; C=comparison, control, or comparator; O=outcome [s]) to frame the literature review (Box 1).

Experts in literature searches from the ACOG Resource Center searched the Cochrane Library, MEDLINE (through Ovid), and PubMed (for references not indexed through MEDLINE) for articles published between January 2000 and October 2021. Literature was organized by types of studies. Published guidelines were categorized separately from studies. A primary reviewer was assigned to each topic to review titles and abstracts and then the entire manuscript when appropriate. Reference lists from relevant articles found in the search were also reviewed. Reviewers did additional searches as necessary, including extending the search range. Internet searches were performed with standard search engines to seek guidelines, recommendations, and tools that might not have been published in peer-reviewed publications. Relevant information was evaluated and compiled into an evidence summary template by a primary reviewer. Completed templates were then reviewed by a secondary reviewer. The primary and secondary reviewers worked together to revise the evidence summary in response to the secondary reviewer's comments.

The ACOG convened the Ovarian Cancer Evidence Review Conference virtually on February 9–10, 2022, bringing together expert panel members and representatives from stakeholder professional and patient advocacy organizations (Appendix 1, http://links.lww.com/AOG/D170). The panel members who served as primary reviewers for each of the research topics prerecorded their presentations, which were viewed in advance by meeting participants, including the stakeholder representatives. Meeting attendees also reviewed the evidence review summaries. At the meeting, expert panel members presented a brief summary of their evidence review findings, which was followed by an open comment and discussion period with conference attendees. Comments were integrated into the evidence review summary by the primary reviewer. The revised summaries were sent to the secondary reviewer for final review, and final revisions were made by the primary reviewer (Appendices 2–8, http://links.lww.com/AOG/D170). The final evidence review summaries were used to develop the educational material (available online at acog.org).

During the performance of the review, there was significant overlap between the results of the literature searches for the research questions about risk factors and risk reduction. The appendices for these two topics present the full evidence summary for each (Appendices 3 and 4, http://links.lww.com/AOG/D170). For this executive summary, epidemiologic and retrospective studies from both searches are combined in the Risk Factors section, and the Risk Reduction section contains summaries of intervention trials and recommendations. Major professional society guidelines cited in the evidence reviews were replaced with the most current versions during the executive summary preparation.

When reporting results of individual studies, we used the terminology describing gender, race, and ethnicity from the source article. Studies almost uniformly used "women" or "females" to refer to the gender of those affected by ovarian cancer. Although ovarian cancer can affect individuals of different sexes who have ovaries, we used "women" or "females" in this review to reflect the cited literature. In keeping with the most common categories of race and ethnicity used in national data collection, when we had a choice of terminology, we used "Black" in place of "non-Hispanic Black" or "African American" and "White" in place of "non-Hispanic White" or "Caucasian." We used "Hispanic," not "Latinx," because "Latinx" was rarely used in any of the articles reviewed. Although some studies restricted their

Box 1. Research Questions and PICO Criteria Used to Frame the Literature Review*

1. Epidemiology of ovarian cancer
   a. Types of ovarian cancer: What is the incidence of ovarian cancer and whom does it affect?
   b. What is the effect of age on ovarian cancer risk? How strong are these risks (quantitate magnitude of risk, broken down by type of cancer when possible)?
2. Risk factors for ovarian cancer
   a. What lifestyle factors are risk factors for ovarian cancer? How strong are these risks?
   b. What hormonal factors are risk factors for ovarian cancer? How strong are these risks?
   c. What family health history factors are risk factors for ovarian cancer? How strong are these risks?
   d. What health history factors are risk factors for ovarian cancer? How strong are these risks?
3. Prevention and risk reduction for ovarian cancer
   a. Which interventions are effective at reducing ovarian cancer in women at average and high risk (attempt to quantify magnitude of risk reduction)?
4. Screening for ovarian cancer
   a. What is the evidence against screening asymptomatic women at average risk?
   b. Are there subgroups at high risk who benefit from screening? How can women at high risk be identified?
   c. How should screening be performed in subgroups at high risk?
5. Early detection
   a. What are common presenting symptoms among women diagnosed with ovarian cancer? How predictive are these presenting symptoms of ovarian cancer?
   b. In premenopausal patients with symptoms, who should undergo evaluation for ovarian cancer? What are the most effective methods of evaluation for ovarian cancer?
   c. In postmenopausal patients with symptoms, what are the most effective methods of evaluation for ovarian cancer?
   d. In asymptomatic patients with an incidental finding of an ovarian cyst on transvaginal ultrasonography or computed tomography, who should undergo evaluation for ovarian cancer? What are the most effective methods of evaluation for ovarian cancer?
6. Health disparities in ovarian cancer
   a. What groups experience inequities and disparities in the ovarian cancer care continuum, and what are those observed disparities?
   b. What factors contribute to health disparities in ovarian cancer?
   c. How can health disparities in ovarian cancer be mitigated so that optimal care and desirable outcomes are shared by populations experiencing health disparity?
7. Overview of diagnosis and care coordination for the primary care practitioner
   a. Unified summary of guidelines and non–guideline-driven standard of care, including
      i. Standard care evaluation of symptoms and incidentally found masses
      ii. Criteria for referral to gynecologic oncologist subspecialist
      iii. Brief summary of what will likely happen after referral at the level for primary care practitioner to set expectations and to provide anticipatory guidance for patient
8. Special considerations
   a.What special considerations do primary care practitioners need to be aware of throughout the ovarian cancer care continuum? How influential are these factors in the patient experience and outcome?

P=patient, problem, or population; I=intervention; C=comparison, control, or comparator; O=outcome(s).
*See Appendices 2–8, http://links.lww.com/AOG/D170, for PICO criteria used for each outline question.

analysis to Hispanic White individuals, others included Hispanic individuals of any race. Given the lack of consistency in the literature, we used "Hispanic" without reference to race.

EPIDEMIOLOGY AND CLASSIFICATION

High-grade serous carcinomas represent the majority of ovarian cancers; however, most do not arise from the ovary but from the fallopian tube.[7] The term "ovarian cancer" is used throughout this review and represents a constellation of malignancies involving the ovary, peritoneum, and fallopian tube.

The lifetime risk of developing ovarian cancer to age 95 years is about 1.1%. In 2018, 235,081 women in the United States were living with the disease. It is estimated that in 2022 there were 19,880 new cases in the United States.[4] An estimated 12,810 women died of ovarian cancer in the United States in 2022.[6]

Stage at diagnosis is typically advanced, with only 19% of cases localized on presentation and at least half of cases presenting with distant disease.[6] Overall 5-year survival in the United States is 49.7% and is strongly correlated with stage at the time of diagnosis. Five-year survival is 93.1%, 74.2%, 30.8%, and 28.2% when stage at the time of diagnosis is localized, regional, distant, and unstaged, respectively.[4] Recurrence risk correlates strongly with stage at diagnosis. Fewer than 10% of women with stage I disease will have recurrence, whereas 90% of women with stage IV disease will have recurrent disease.[8]

Ovarian cancers are classified by the tissue from which they originate: epithelial, germ cell, and sex cord–stromal. Epithelial cancer is by far the most common, accounting for 90% of malignant ovarian neoplasms. Germ-cell tumors represent about 5% of ovarian cancers, and sex cord–stromal tumors account for 3–5%. All of these types can be further subdivided (Box 2).[5,9–11]

New cases of ovarian cancer in the United States have been falling by an average of 3.3% each year since 2009, and age-adjusted death rates have been falling by about 2.7% annually since 2010[4] (Appendix 2, http://links.lww.com/AOG/D170, provides a complete evidence summary). Incidence and mortality by race and ethnicity are reviewed in detail in the companion article, "Health Disparities in Ovarian Cancer: Report from the Ovarian Cancer Evidence Review Conference."[12]

Box 2. Ovarian Cancer Types

Epithelial ovarian cancer
- Serous carcinoma
  - –High-grade serous carcinoma
  - –Low-grade serous carcinoma
- Endometrioid carcinoma
- Mucinous carcinoma
- Clear-cell carcinoma
- Borderline or low-malignant-potential neoplasms
- Carcinosarcoma
- Undifferentiated or dedifferentiated
- Transitional cell carcinoma (Brenner tumor)

Germ-cell tumors
- Dysgerminoma
- Immature teratoma
- Embryonal carcinoma
- Endodermal sinus or yolk sac tumors

Sex cord–stromal tumors
- Granulosa cell tumors
- Thecomas
- Sertoli-Leydig cell tumors

RISK FACTORS

Age

With some exceptions, ovarian cancer is generally a disease of older age, with more than 88% of cases diagnosed after age 45 years.[4] For children and young adults, the incidence of malignant ovarian cancer of any type is very low. Girls and young women aged 0–14 years, 15–19 years, and 20–24 years have an incidence of only 3.7, 13.7, and 17.3 cases per 1,000,000 females, respectively.[13] Overall incidence of ovarian cancer increases over a woman's lifetime, peaking in the seventh decade of life, with a median age at diagnosis of 63 years.[4,5] The age at peak incidence varies significantly by histologic type; for germ-cell ovarian cancers, it is in the second decade of life; for sex cord–stromal ovarian cancers, it is in the sixth decade; for epithelial ovarian cancers, peak incidence occurs in the seventh and eighth decades.[14]

Lifestyle

No specific diet has been consistently associated with increases or decreases in the risk of ovarian cancer. Current data do not show an increased risk of ovarian cancer with alcohol use.[15–17] Although a number of reviews and individual studies of obesity and the risk of ovarian cancer have shown an association, results have been inconsistent,[18–20] possibly because of unmeasured obesity-related confounding risk factors. Increased physical activity has been associated with decreased risk of ovarian cancer, and inactivity has been associated with increased risk. The strongest data supporting an inverse association between physical activity and the risk of ovarian cancer come from case–control studies. In a review, data from included

case–control studies demonstrated risk reductions of at least 20% among women who are regularly active.[21] Some studies report an association between smoking and increased risk of mucinous ovarian cancer and decreased risk of clear-cell carcinoma. These associations have been difficult to study given the small number of cases and the many subtypes of ovarian cancer.[22] Our review found heterogeneity in the studies on the use of talcum powder and ovarian cancer risk (Appendix 3, http://links.lww.com/AOG/D170, provides a complete evidence summary).

Hormonal

Endogenous Hormones

In a population-based, case–control study, parous women had a significant reduction of ovarian cancer risk (odds ratio [OR] 0.4, 95% CI 0.3–0.6 vs nulliparous women).[23] Later age at menarche and earlier age at menopause have been shown to significantly decrease the risk of ovarian cancer. In a case–control study, the OR was 0.8 (95% CI 0.6–1.0) for women reporting menarche at age 15 years or older compared with women reporting menarche at age 12 years or younger.[24] Women who reported menopause before age 45 years had an OR of ovarian cancer of 0.6 (95% CI 0.5–0.9) compared with women who reported menopause at age 45 years or older.[24]

Breastfeeding appears to have a protective effect for women at both average and high risk.[25,26] In women at average risk, a meta-analysis of 19 studies including a total of 469,095 women reported a 24% reduction in ovarian cancer among those who breastfed (95% CI 0.69–0.83), and a longer duration of breastfeeding was associated with decreased risk of ovarian cancer.[26] In a 2021 systematic review and meta-analysis investigating breastfeeding and the risk of ovarian cancer in *BRCA1* and *BRCA2* mutation carriers, the overall pooled OR of ever having breastfed among patients who had ovarian cancer was 0.767 (95% CI 0.688–0.856) for patients with *BRCA1* mutations and 0.817 (95% CI 0.650–1.028) for patients with *BRCA2* mutations.[27] In a study of two prospective cohorts, breastfeeding for 18 months or more compared with never breastfeeding was associated with a significantly decreased risk of ovarian cancer (relative risk [RR] 0.66, 95% CI 0.46–0.96). For each month of breastfeeding, the RR decreased by 2% (RR 0.98, 95% CI 0.97–1.00).[28]

Menopausal Hormone Therapy

Postmenopausal hormone therapy (HT) has consistently been associated with an increased risk of ovarian cancer. In a meta-analysis of 42 studies that included 12,238 cases of ovarian cancer, estrogen-only HT was associated with a 1.28-fold increased risk (95% CI 1.18–1.40) of developing epithelial ovarian cancer, and estrogen–progestin HT was associated with a 1.11-fold (95% CI 1.02–1.21) increased risk.[29] Guidelines for the use of HT were beyond the scope of our evidence review. Use of HT requires a much broader assessment of risks and benefits than included here.

Combined Oral Contraceptives

Multiple studies and systematic reviews have consistently shown decreased ovarian cancer risk with hormonal contraceptive use in women at average and high risk.[30–34] In women at average risk, a 2013 meta-analysis noted a significant reduction in ovarian cancer incidence in ever-users compared with never-users of oral contraception (OR 0.73, 95% CI 0.66–0.81), with a 50% reduction noted after 10 or more years of use.[35] In an analysis of six case–control studies, the risk reduction in ovarian cancer increased with longer duration of oral contraceptive use (OR 0.83, 95% CI 0.69–1.01 for use for less than 5 years; OR 0.42, 95% CI 0.30–0.59 for use for 5 years or longer vs nonuse).[36] In women at high risk, a meta-analysis of 18 studies involving 1,503 cases of ovarian cancer found that oral contraceptive use was associated with a significantly reduced risk of ovarian cancer in women with a *BRCA1* or *BRCA2* mutation (summary RR 0.50, 95% CI 0.33–0.75), with an additional risk reduction of 36% for each additional 10 years of use (RR 0.64, 95% CI 0.53–0.78).[37] In another meta-analysis of three case–control studies, there was a significantly reduced risk of ovarian cancer in *BRCA1* and *BRCA2* mutation carriers with any past use of combined oral contraceptives (OR 0.57, 95% CI 0.47–0.70). This same study also demonstrated a reduced ovarian cancer risk with a longer duration of use (OR 0.95, 95% CI 0.93–0.97; $P<.001$).[38]

Intrauterine Devices and Progesterone-Only Contraception

A 2021 meta-analysis that included three prospective cohort studies found no difference in cancer risk between levonorgestrel intrauterine system users and never-users (OR 0.66, 95% CI 0.41–1.08).[39] A second meta-analysis of 11 studies found decreased risk with intrauterine device use (OR 0.68, 95% CI 0.62–0.75). However, this study pooled all types of intrauterine devices and combined both cohort and case–control studies.[40] In a prospective cohort study of women from Denmark, use of progesterone-only contraceptives was not associated with ovarian cancer risk

(276,221 person-years, adjusted RR 0.87, 95% CI 0.59–1.29).[41]

Tubal Ligation

Tubal ligation is associated with decreased risk of ovarian cancer. In a meta-analysis of 13 studies, having a tubal ligation was associated with a 34% decreased risk of epithelial ovarian cancer (RR 0.66, 95% CI 0.60–0.73).[42]

Family History and Genetic Mutations

The risk of ovarian cancer is increased with certain genetic mutations. About 10–25% of ovarian cancers are associated with a hereditary genetic abnormality.[9] Although multiple germline mutations are associated with ovarian cancer, *BRCA1* and *BRCA2* germline mutations are the most common and are found in 10–15% of women with ovarian cancer.[9,43,44] A woman with a *BRCA1* mutation has a 39–58% lifetime risk of ovarian cancer, whereas a woman with a *BRCA2* mutation has about a 13–29% lifetime risk.[45] *BRIP1*, *RAD51C*, and *RAD51D* have also been associated with an increased risk of ovarian cancer. Mutations in these three genes are estimated to be associated with 2% of ovarian cancer cases.[46] Other genetic mutations and the absolute risk of epithelial ovarian cancer are shown in Table 1.[45]

Table 1. Ovarian Cancer Risk by Genetic Mutation

Gene	Epithelial Ovarian Cancer Absolute Risk*
ATM	<3%
BRCA1	39%–58%
BRCA2	13%–29%
BRIP1	>10%
MLH1, MSH2	>10%
MSH6	≤13%
PMS2	<3%
EPCAM	<10%
PALB2	3%–5%
RAD51C	>10%
RAD51D	>10%

* Modified with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for genetic/familial high-risk assessment: breast, ovarian and pancreatic v2.2022. © 2022 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available. NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Family history of ovarian cancer without an identified inherited genetic mutation is also associated with increased ovarian cancer risk. In a case–control study that included 554 patients, ovarian cancer in a first-degree relative (mother or sister) was associated with a 2.4-fold increased risk (95% CI 1.4–4.1).[47,48]

Health History

Infertility

A 2020 meta-analysis including nine prospective cohort studies and 10,383 patients with ovarian cancer found that the RR of ovarian cancer was 1.51 (95% CI 1.35–1.69) in patients with infertility with low heterogeneity.[49] It is not clear whether infertility is an independent risk factor or whether the observed effect is mediated by nulliparity, endometriosis, decreased contraceptive use, and other risk factors. The American Society for Reproductive Medicine guideline states that, according to available data, there is no significant increased risk of ovarian cancer after the use of fertility drugs, but there potentially may be a small increased risk of borderline ovarian tumors.[50] In a large cohort study evaluating the incidence of borderline ovarian tumors in patients undergoing in vitro fertilization (IVF) identified through a hospital registry, the rate of borderline ovarian tumors in women undergoing IVF compared with patients not undergoing IVF was higher with a hazard ratio of 2.46 (95% CI 1.20–5.04).[51] Similarly, in another cohort of more than 19,000 women undergoing IVF, compared with the general population, the incidence of borderline tumors was higher (standardized incidence ratio 1.76, 95% CI 1.16–2.56).[52]

Endometriosis

Consistent data suggest an association between endometriosis and invasive ovarian carcinoma. In a meta-analysis including 40,609 cases of ovarian cancer, Wang et al[53] found an association between endometriosis and epithelial ovarian cancer (OR 1.42, 95% CI 1.28–1.57). There appears to be a stronger association of endometriosis with clear-cell carcinoma.[53–56]

Other Medications

Aspirin use has been associated with a slightly lower risk of ovarian cancer in observational studies[57,58] (Appendices 3 and 4, http://links.lww.com/AOG/D170, provide complete evidence summaries involving risk factors). In a large cohort study using Korean National Health Insurance Service data, β-blocker use has also been associated with better survival outcomes in ovarian cancer in cases of long-term duration of use and in older patients.[59]

RISK REDUCTION

A 2009 meta-analysis showed an 80% reduction in the incidence of ovarian cancer after risk-reducing bilateral salpingo-oophorectomy (BSO) in *BRCA1* and *BRCA2* carriers (95% CI 0.12–0.39).[60] Risk-reducing BSO is recommended by ACOG, the National Comprehensive Cancer Network, and the Society of Gynecologic Oncology for women at increased risk of ovarian cancer (Box 3).[45,61,62] Several studies have explored the safety of the procedure and concerns about the effects of estrogen deprivation and quality of life.[63–65] Other than an increase in hot flushes and vaginal dryness, there were no reported significant risks to the procedure.

Although the feasibility of complete salpingectomy compared with standard postpartum tubal ligation at cesarean delivery has been demonstrated,[66] our review did not find any prospective studies of ovarian cancer risk reduction with opportunistic salpingectomy alone among either women at high risk or

Box 3. Recommendations for Ovarian Cancer Risk Reduction

National Comprehensive Cancer Network*

Risk-reducing BSO:

- "*BRCA* pathogenic/likely pathogenic variant-positive management: Recommend risk-reducing salpingo-oophorectomy, typically between 35 and 40 years, and upon completion of childbearing. Because ovarian cancer onset in patients with *BRCA2* pathogenic/likely pathogenic variants is an average of 8–10 years later than in patients with *BRCA1* pathogenic/likely pathogenic variants, it is reasonable to delay RRSO for management of ovarian cancer risk until age 40–45 years in patients with *BRCA2* pathogenic/likely pathogenic variants unless age at diagnosis in the family warrants earlier age for consideration of prophylactic surgery." (page BRCA-A 2 of 3)
- Consider between the ages of 45 and 50 years in carriers of a *BRIP1* variant (12% lifetime risk), an *RAD51C* variant (11% lifetime risk), and an *RAD51D* variant (13% lifetime risk).
- Total hysterectomy or BSO may be considered in those who have completed childbearing and carry a mismatch repair gene linked to Lynch syndrome.

SDO: Salpingectomy alone is not recommended for risk reduction.

Society of Gynecologic Oncology†

Risk-reducing BSO: Recommend risk-reducing BSO "be performed between 35 and 40 years of age in women with *BRCA1* and *BRCA2* mutations. Guidance for women who are at high risk according to strong family histories or who have been identified with a genetic mutation other than *BRCA1* or *BRCA2* generally follows the guidelines for *BRCA1* and *BRCA2* mutation carriers, but there are fewer data for these groups to support the value of salpingo-oophorectomy. Some syndromes such as Peutz-Jeghers syndrome are associated with cancer at a younger age, so the timing of RRSO should be individualized according to the age of incident cancers in the family or the specific mutation. Flexibility in the timing of RRSO may also be appropriate for *BRCA2* carriers who present with ovarian cancer at a later age than BRCA1 carriers." (page 2112)

SDO: "Can be considered at the completion of childbearing in women at increased genetic risk of ovarian cancer who do not agree to salpingo-oophorectomy. However, this is not a substitute for oophorectomy, which should still be performed as soon as the woman is willing to accept menopause, preferably by the age of 40 years." (page 2116)

OS: "Can be considered in average-risk women undergoing hysterectomy, other pelvic surgery, or sterilization at the completion of childbearing." (page 2116)

OC use: "Women with *BRCA1* or *BRCA2* mutations should consider taking oral contraceptive pills to reduce their ovarian cancer risk." (page 2112)

American College of Obstetricians and Gynecologists‡

Risk-reducing BSO: recommend at age 35–40 years for *BRCA1* mutation carriers; women with *BRCA2* mutations may consider delaying until age 40–45 years.

OS: Salpingectomy at the time of hysterectomy or as a means of tubal sterilization appears to be safe and does not increase the risk of complications. OS should not alter the intended route of hysterectomy.

OC use: Appropriate for women with mutations in *BRCA1* or *BRCA2* if indicated. Use for cancer prophylaxis is reasonable.

BSO, bilateral salpingo-oophorectomy; RRSO, risk-reducing salpingo-oophorectomy; SDO, salpingectomy with delayed oophorectomy; OS, opportunistic salpingectomy; OC, oral contraceptive.

*National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Genetic/familial high-risk assessment: breast, ovarian, and pancreatic version 2.2021. Accessed May 15, 2022. https://nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf

†Walker JL, Powell CB, Chen LM, Carter J, Bae Jump VL, Parker LP, et al. Society of Gynecologic Oncology recommendations for the prevention of ovarian cancer. Cancer 2015;121:2108–20. doi: 10.1002/cncr.29321

‡Hereditary breast and ovarian cancer syndrome. Practice Bulletin No. 182. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;130:e110–26. doi: 10.1097/AOG.0000000000002296

those at average population risk. Existing retrospective data support that bilateral salpingectomy is at least comparable, if not superior, to bilateral tubal ligation for reducing ovarian cancer risk.[42,67] A meta-analysis from 2016 reported a significantly reduced risk of ovarian cancer in women who underwent bilateral salpingectomy compared with those who did not (OR 0.51, 95% CI 0.35–0.75).[68]

Our review did not identify data to support salpingectomy alone in women at high risk. Anecdotal evidence of an increase in the number of women at high risk being offered salpingectomy with delayed oophorectomy indicates that there is a potential false perception of decreased risk in these patients after salpingectomy, which may ultimately decrease the odds of their timely return for ovary removal.[69,70] Multiple studies are underway to evaluate the risks and benefits of salpingectomy with delayed oophorectomy in women at high risk for ovarian cancer.[71,72]

Epidemiologic evidence for potentially modifiable risk factors is summarized in the Risk Factor section. Our search found no interventional studies addressing these risk factors and no specific guidance from major professional societies. Given the well-accepted health benefits of contraception, physical activity, and lactation, it is reasonable to counsel patients on the potential secondary benefits of these activities on ovarian cancer risk (Appendix 4, http://links.lww.com/AOG/D170, provides a complete evidence summary).

SCREENING

Screening Methods That Have Been Proposed

The most common methods studied for ovarian cancer screening are transvaginal ultrasonography, bimanual palpation, and measurement of the serum tumor marker CA 125. Algorithms using a combination of transvaginal ultrasonography and tumor markers have also been studied. These algorithms include the ROCA (Risk of Ovarian Cancer Algorithm)[73] and the parametric empirical Bayes model. ROCA estimates the risk of ovarian cancer on the basis of age and change in CA 125. The algorithm makes recommendations for repeat assessment of CA 125 or transvaginal ultrasonography on the basis of the calculated risk. ROCA was initially studied in a randomized controlled trial of 13,582 women aged 50 years and older; ROCA had a specificity for epithelial ovarian cancer of 99.8% (95% CI 99.7–99.9%) and a positive predictive value of 19% (95% CI 4.1–45.6%).[73] ROCA was further studied in the prospective United Kingdom Familial Ovarian Cancer Screening Study and in a large-scale, randomized controlled trial in the United Kingdom.[74,75] The parametric empirical Bayes model also interprets serial CA 125 levels and has performed similarly to ROCA in an examination of U.K. data sets.[76]

Screening in Asymptomatic Women at Average Risk

In our review, no major professional society has recommended the use of ovarian cancer screening in asymptomatic women at average risk, nor did any individual study show clear overall benefit. Several large randomized controlled trials have examined ovarian cancer screening in patient populations at average risk. These studies include the Shizuoka Cohort Study of Ovarian Cancer Screening in Japan; the PLCO (Prostate, Lung, Colorectal, and Ovarian Cancer) screening trial in the United States; the UKCTOCS (UK Collaborative Trial of Ovarian Cancer Screening); and the U.K. pilot study that preceded the UKCTOCS. These trials have been included in several systematic reviews and meta-analyses. A 2018 systematic review was conducted by the U.S. Preventive Services Task Force for its updated publication on screening for ovarian cancer and included results from the UKCTOCS, the smaller U.K. pilot trial, and the PLCO trial. This systematic review did not include information from the Shizuoka Cohort Study in Japan because of the lack of mortality data and the significantly lower prevalence of ovarian cancer (0.31/1,000) than expected in the U.S. population.[77] The systematic review found that screening offered no benefit in terms of ovarian cancer mortality. It found that the screened group in the PLCO trial had an RR of mortality of 1.18 (95% CI 0.82–1.71) compared with the control groups, whereas the UKCTOCS trial had hazard ratios of 0.91 (95% CI 0.76–1.09) for the ultrasonography-screened group and 0.89 (95% CI 0.74–1.08) for the CA 125-screened group. A meta-analysis by Marchetti et al[78] in 2018 evaluated data on postmenopausal, asymptomatic women using data from the PLCO trial, the Shizuoka Cohort Study, and the UKCTOCS. Although the meta-analysis showed earlier stage of diagnosis with ovarian cancer screening compared with unscreened individuals in a control group (RR 1.30, 95% CI 1.14–1.49), it did not show a benefit of screening for disease-specific mortality (RR 0.96, 95% CI 0.85–1.10).[78] The meta-analysis found an increase in ovarian cancer diagnoses when the multimodal approach of CA 125 assessment with follow-up ultrasonography was performed (RR 1.39, 95% CI 1.21–1.60).[78]

Our review did not find any high-quality evidence supporting the use of other serum markers,

circulating tumor cells, or algorithms in ovarian cancer screening. The U.S. Preventive Services Task Force recommends against screening for ovarian cancer in asymptomatic women who are not known to have a high-risk hereditary cancer syndrome, concluding that "there is at least moderate certainty that the harms of screening for ovarian cancer outweigh the benefits."[79]

Screening in Patients at High Risk

We found no randomized controlled trials of ovarian cancer screening in women at high risk. Secondary analysis of the PLCO cancer screening trial data revealed similar rates of abnormal ovarian cancer screening with ultrasonography and CA 125 evaluation across all risk groups and no difference in overall or disease-specific mortality.[80,81] The University of Kentucky Ovarian Cancer Screening Trial, which used screening ultrasonography and CA 125 assessment, reported increased 5- and 10-year survival rates for patients with screening-detected epithelial ovarian cancer compared with unscreened patients with epithelial ovarian cancer; however, this study was not randomized, lacked a control group, and did not describe patients' cancer histology.[82,83]

Because of the lack of efficacy of ovarian cancer screening in patients at high risk, none of the professional societies included in this review explicitly recommend ovarian cancer screening for this population; however, several state that ovarian cancer screening can be offered to patients at high risk (Table 2).

Several organizations support identifying women at high risk. The ACOG, the National Comprehensive Cancer Network, the National Institute for Health and Care Excellence, and the Society of Obstetricians and Gynaecologists of Canada recommend genetic counseling on the basis of family history of breast or ovarian cancer or both (Table 2).[45,61,84–90] High-risk women can be identified by cancer risk assessments that include all cancers in the family history. Genetic testing can then discover pathogenic mutations in genes that increase the risk of epithelial ovarian cancer. Currently, the National Comprehensive Cancer Network lists *ATM*, *BRCA1*, *BRCA2*, *BRIP1*, *DICER1*, *EPCAM*, *MLH1*, *MSH2*, *MSH6*, *PALB2*, *PMS2*, *RAD51C*, and *RAD51D* as genes associated with moderate or high risk for ovarian cancer[45] (Appendix 5, http://links.lww.com/AOG/D170, provides a complete evidence summary).

EARLY DIAGNOSIS

In a systematic review of published studies of symptoms associated with ovarian cancer, the presence of an abdominal mass (positive likelihood ratio [LR] 30.0), abdominal distention or increased girth (positive LR 16.0), and abdominal or pelvic pain (positive LR 10.4) had the highest LRs associated with an ovarian cancer diagnosis. The specificities associated with these symptoms range from 88% to 99%; however, the sensitivities were all less than 50%.[91] Indices have been developed that combine symptoms and their duration to improve prediction. The Goff Ovarian Cancer Symptom Index (combined sensitivity 63%, specificity 95%, positive LR 12.6) and the Grewal symptom score (combined sensitivity 73%, specificity 91%, positive LR 8.37) have been independently validated.[91] According to a secondary analysis of UKCTOCS data, survival appears to be worse in patients who report more than one symptom at the time of diagnosis and in those who met criteria for a symptom index.[92]

Professional society guidelines about when to initiate an evaluation on the basis of symptoms vary. The ACOG states that patients and clinicians "should maintain an appropriate level of suspicion when … signs and symptoms of ovarian cancer are present."[93] Ultrasonography of the pelvis (transabdominal and transvaginal with duplex Doppler) is the most frequently recommended imaging modality for the evaluation of patients with symptoms.[10,11,94–98] The U.K. National Institute for Health and Clinical Excellence guidelines differ in that they recommend that clinicians "measure serum CA 125…in women with symptoms that suggest ovarian cancer. If serum CA 125 is 35 international units/mL or greater, arrange an ultrasound scan of the abdomen and pelvis."[96] We found no high-quality studies comparing imaging, biomarkers, risk algorithms, or multimodal risk assessment tools for the primary evaluation of patients with symptoms associated with ovarian cancer.

Appendix 6, http://links.lww.com/AOG/D170, summarizes studies and society guidelines for patients with an incidental finding of an ovarian cyst on imaging using various methods, including transvaginal ultrasonography, biomarkers, biomarker assays, and multimodal risk assessment, to exclude ovarian cancer. The studies had a number of limitations, including being conducted in patients who underwent surgery, limiting understanding of how the strategies perform in expectantly managed patients.[99] The study populations also frequently had a higher ovarian cancer incidence than expected, which may overestimate diagnostic accuracy.[99] CA 125 is the most frequently measured serum marker for the evaluation and early diagnosis of ovarian cancer despite variation in its measured sensitivity (61–90%) and specificity (71–

Table 2. Identification and Screening of High-Risk Patients

Source	Recommendations
ACOG*	Recommends genetic counseling based on family and personal histories Routine ovarian cancer screening is not recommended, but transvaginal ultrasonography or CA 125 level assessment can be considered starting at age 30–35 y until RRSO. No consensus on ovarian cancer screening in patients with Lynch syndrome
ACR 2017 Appropriateness criteria†	No effective ovarian cancer screening Ovarian cancer screening with pelvic ultrasonography may be appropriate for some premenopausal or postmenopausal women at increased risk for ovarian cancer, which includes those with a personal history or family history of ovarian cancer, known or suspected genetic predisposition, or elevated CA 125 level.
ASRM/SGO‡	No strong evidence for effective ovarian cancer screening Transvaginal ultrasonography and CA 125 level assessment may be an option for women who decline or defer RRSO.
ESMO§	No strong evidence for effective ovarian cancer screening Transvaginal ultrasonography and CA 125 every 6 mo can be considered from age 30 with proper counseling on the lack of efficacy.
NCCN‖	Recommends genetic counseling based on family and personal histories No strong evidence for effective ovarian cancer screening If RRSO is not chosen, transvaginal ultrasonography and CA 125 assessment for ovarian cancer screening may be considered starting at age 30–35.
NICE¶	Recommends a risk assessment for patients with a family history of ovarian cancer or breast cancer in first- or second-degree relatives
RCOG#	Ovarian cancer screening should not be offered as an alternative to RRSO.
SOGC**	Recommends genetic counseling No strong evidence for effective ovarian cancer screening

ACOG, American College of Obstetricians and Gynecologists; RRSO, risk-reducing salpingo-oophorectomy; ACR, American College of Radiology; ASRM, American Society for Reproductive Medicine; SGO, Society of Gynecologic Oncology; ESMO, European Society for Medical Oncology; NCCN, National Comprehensive Cancer Network; NICE, National Institute for Health and Care Excellence; RCOG, Royal College of Obstetricians and Gynaecologists; SOGC, Society of Obstetricians and Gynaecologists of Canada.

* Hereditary breast and ovarian cancer syndrome. Practice Bulletin No 182. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;130:e110–26. doi:10.1097/AOG.0000000000002296; *and* Lynch syndrome. Practice Bulletin No. 147. American College of Obstetricians and Gynecologists and the Society of Gynecologic Oncology. Obstet Gynecol 2014;124:1042–54. doi:10.1097/01.AOG.0000456325.50739.72

† Expert Panel on Women's Imaging; Pandharipande PV, Lowry KP, Reinhold C, Atri M, Benson CB, et al. ACR Appropriateness Criteria® Ovarian Cancer Screening. J Am Coll Radiol 2017;14:S490–9. doi: 10.1016/j.jacr.2017.08.049

‡ Chen L, Blank SV, Burton E, Glass K, Penick E, Woodard T. Reproductive and hormonal considerations in women at increased risk for hereditary gynecologic cancers: Society of Gynecologic Oncology and American Society for Reproductive Medicine evidence-based review. Fertil Steril 2019;112:1034–42. doi:10.1016/j.fertnstert.2019.07.1349

§ Paluch-Shimon S, Cardoso F, Sessa C, Balmana J, Cardoso MJ, Gilbert F, et al. Prevention and screening in BRCA mutation carriers and other breast/ovarian hereditary cancer syndromes: ESMO Clinical Practice Guidelines for cancer prevention and screening. Ann Oncol 2016;27(suppl 5):v103–10.

‖ National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Genetic/familial high-risk assessment: breast, ovarian, and pancreatic version 2.2021. Accessed May 15, 2022. https://nccn.org/login?ReturnURL=https://nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf

¶ National Institute for Health and Care Excellence. Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer. Clinical Guideline 164. 2013, updated 2019. Accessed April 8, 2022. https://www.nice.org.uk/guidance/cg164

Management of women with a genetic predisposition to gynaecological cancers. Scientific Impact Paper No. 48. Royal College of Obstetricians and Gynaecologists. Obstet Gynaecol 2015;17:140. doi: 10.1111/tog.12182

** Jacobson M, Bernardini M, Sobel ML, Kim RH, McCuaig J, Allen L. Gynaecologic management of heeditary breast and ovarian cancer. Committee Opinion No. 366. Society of Obstetricians and Gynaecologists of Canada. J Obstet Gynaecol Can 2018;40:1497–510. doi: 10.1016/j.jogc.2018.05.046

93%).[94] Sensitivity and specificity are poorer in premenopausal patients than postmenopausal patients, likely because benign conditions that can cause CA 125 elevation occur more frequently in premenopausal patients than postmenopausal patients and the ovarian cancer incidence is lower in premenopausal patients than in postmenopausal patients.[94]

The International Ovarian Tumour Analysis Phase 5 study was a prospective, multicenter cohort study with patients selected for surgery or conservative management on the basis of morphology and symptoms.[100] In this study, 1,919 patients with a new diagnosis of a mass that was assessed as benign on ultrasonography had outcomes examined at 24 months after

enrollment. Of these, 20.2% had spontaneous resolution of their mass during follow-up, and 16.1% had surgical intervention. The risk of a missed diagnosis at surgery was less than 0.5% when defined as a final diagnosis of invasive malignancy, borderline tumor, torsion, or cyst rupture. We found no prospective studies to guide the frequency or duration of ultrasound surveillance.

We found several relevant guidelines for the management of incidentally identified masses. According to the ACOG, "transvaginal ultrasonography is the recommended imaging modality for a suspected or and incidentally identified pelvic mass. No alternative imaging modality has demonstrated sufficient superiority to transvaginal sonography to justify routine use."[94] The American College of Radiology's Ovarian-Adnexal Reporting and Data System ultrasound risk-stratification and management system recommends ultrasound follow-up, referral to an ultrasound specialist, pursuing magnetic resonance imaging, or referral to a gynecologist or gynecologic oncologist on the basis of the risk of malignancy[101] (Table 2 in Appendix 6, http://links.lww.com/AOG/D170, gives more information).

Most relevant guidelines, including the National Institute for Health and Care Excellence, the European Society for Medical Oncology, the Royal College of Obstetricians and Gynaecologists, and the Society of Obstetricians and Gynaecologists of Canada, make no mention of use of serum biomarker panels.[10,96–98] The ACOG states, "Serum biomarker panels may be used as an alternative to CA 125 level alone in determining the need for referral to or consultation with a gynecologic oncologist when an adnexal mass requires surgery. These biomarker panels are not recommended for use in the initial evaluation of an adnexal mass, but may be helpful in assessing which women would benefit from referral to a gynecologic oncologist"[94] (Appendix 6, http://links.lww.com/AOG/D170, gives a complete evidence summary).

HEALTH DISPARITIES

Significant ovarian cancer health disparities were noted in the evidence review across the continuum of care and are often linked to nonadherence to guidelines from the National Comprehensive Cancer Network. Black patients, those with low socioeconomic status, and those who do not have private insurance are among the populations who often receive less treatment.

Black women consistently had worse outcomes and less improvement in survival over time compared with their White counterparts. We found little evidence regarding other racial and ethnic groups (eg, Hispanic White women and Asian and Pacific Islander women) and other socially marginalized populations. Our review found no articles meeting inclusion criteria on ovarian cancer risk among individuals who do not identify as cisgender or female. These findings were important enough that panel members and stakeholder representatives agreed that the topic merits its own summary. Please see the companion summary, "Health Disparities in Ovarian Cancer: Report from the Ovarian Cancer Evidence Review Conference."[12]

DIAGNOSIS AND CARE COORDINATION

Features that help stratify risk of malignancy and guide management include patient characteristics, physical examination findings, imaging results, and serum tumor marker levels.[94] Patient history should include a thorough personal medical and gynecologic history, family history, and review of symptoms.[94] A thorough physical examination should include palpation of cervical, supraclavicular, axillary, and groin lymph nodes; a pulmonary examination; palpation and auscultation of the abdomen; and a pelvic examination with visual inspection of the perineum, cervix, and vagina, as well as a bimanual examination that includes a rectovaginal examination if indicated. Masses that are irregular, firm, fixed, nodular, bilateral, or associated with ascites are more concerning for malignancy.[94]

Transvaginal ultrasonography is typically the most appropriate initial imaging modality for the assessment of adnexal masses. Features that are concerning for malignancy include papillary or solid components, irregularity, presence of ascites, and high color Doppler flow. Magnetic resonance imaging may further distinguish benign from malignant masses, especially if they are indeterminate on ultrasonography, and may help establish the origin if it is not clearly adnexal.[102] Computed tomography is useful to assess for the extent of metastatic disease, to evaluate for a potential other primary site, and to plan for surgery.[94] Baseline blood tests should include a complete blood count, chemistry profile with liver function tests, and tumor marker assessment.

Accurately predicting malignancy in asymptomatic and symptomatic masses is difficult. The National Comprehensive Cancer Network recommends that "because the primary assessment and debulking by a gynecologic oncologist is associated with improved survival, all patients with lesions suspected to be ovarian malignancies (based on clinical evidence) should

be referred to an experienced gynecologic oncologist for evaluation."[5] The ACOG recommends either consultation with or referral to a gynecologic oncologist for those with an adnexal mass who meet one or more of the following criteria:[94]Any patient with ultrasound findings suggestive of malignancy, ascites, a nodular or fixed pelvic mass, or evidence of abdominal or distant metastasisPostmenopausal patient with elevated CA 125 levelPremenopausal patient with a very elevated CA 125 levelAny patient with an elevated score on a formal risk assessment test such as the multivariate index assay, Risk of Malignancy Index, or the Risk of Ovarian Malignancy Algorithm or one of the ultrasound-based scoring systems from the International Ovarian Tumor Analysis Group

Multiple studies have demonstrated that having a gynecologic oncologist involved in the care of patients with ovarian cancer increases survival and offers other advantages. Surgery by a gynecologic oncologist has consistently been associated with higher rate of optimal tumor debulking, improved long-term and overall survival, higher likelihood of undergoing a staging surgery if appropriate, higher likelihood of receiving chemotherapy, and increased likelihood of receiving guideline-concordant care.[103–108]

After referral to a gynecologic oncologist, the trajectory of management typically depends on whether the disease is isolated or metastatic and the individual patient's fertility wishes, functional status, medical comorbidities, and goals. Management decisions for patients with ovarian cancer involve important, complex, and subtle nuances that must be carefully considered.

For patients with apparent early-stage disease, comprehensive surgical staging typically includes a thorough abdominal exploration, aspirating ascites or obtaining pelvic washings, peritoneal biopsies, and omentectomy, with pelvic and para-aortic lymphadenectomy for most histologies except mucinous carcinoma, granulosa cell tumors, and borderline tumors.[5]

For patients with advanced disease, primary tumor debulking surgery and neoadjuvant chemotherapy may be options. This decision is a complex, nuanced one (Appendix 6, http://links.lww.com/AOG/D170). For patients who are good surgical candidates and have metastatic disease that is surgically resectable, surgical debulking is typically recommended. For patients who are poor surgical candidates or in whom the likelihood of a complete surgical cytoreduction is low, neoadjuvant chemotherapy may be appropriate.[5,109] Evaluation by a gynecologic oncologist is recommended to inform this decision before initiation of neoadjuvant chemotherapy. Laparoscopy can also be a useful tool to evaluate the feasibility of optimal cytoreduction.

Consideration of clinical trials whenever possible is recommended for all patients with ovarian cancer.[5] In general, adjuvant chemotherapy is recommended for most patients with ovarian cancer except patients with low-grade stage IA or IB ovarian cancer and those with select histologies.[5] Adjuvant chemotherapy for epithelial cancer typically consists of intravenous carboplatin and paclitaxel. Determining the optimal number of cycles, dosing, and frequency of chemotherapy is complex, so counseling by a gynecologic oncologist is important.[5] Incorporation of bevacizumab and poly (ADP-ribose) polymerase inhibitor maintenance may be considered in advanced disease.[5]

Patients with ovarian cancer, fallopian tube cancer, or primary peritoneal cancer should also have genetic risk evaluation and germline and somatic testing.[5] Because most patients with ovarian cancer will undergo surgery and chemotherapy at some point, the primary care practitioner can play an important role in optimizing the status of the patient to undergo such treatment[5] (Appendix 7, http://links.lww.com/AOG/D170, provides a complete evidence summary).

SPECIAL CONSIDERATIONS

In women in whom early-stage ovarian cancer presents before completion of childbearing, it is appropriate to consider avoiding the traditional radical surgical approach of a hysterectomy, BSO, and comprehensive surgical staging in favor of fertility-sparing surgery, which typically consists of a unilateral salpingo-oophorectomy with surgical staging and allows retention of the unaffected ovary and uterus.[110] When this approach is reserved for patients with early-stage disease, recurrence rates and survival are similar to those found in patients treated with conventional surgery.[110,111] Obstetric outcomes after fertility-sparing surgery typically mirror the baseline population rate.[112] The National Comprehensive Cancer Network recommends considering fertility-sparing surgery for patients who wish to preserve fertility and have apparent early-stage disease or low-risk tumors such as early-stage invasive epithelial tumors, low-malignant-potential lesions, malignant germ-cell tumors, or malignant sex cord–stromal tumors.[5] The American Society of Clinical Oncology also provides guidelines for using fertility-sparing surgery on the basis of histology and stage.[95]

After treatment for ovarian cancer, patients contend with varied residual symptoms, including increased rates of depression and anxiety.[113] Physical symptoms after completion of treatment can include

residual neuropathy, pelvic pain, fatigue, nausea, and decreased libido.[114,115] Sexuality is dramatically affected by surgical treatment for ovarian cancer. In one systematic review, 47% of patients reported little or no sexual desire, 62% reported pain with sex, and 80% reported vaginal dryness.[116] General well-being can also suffer because ovarian cancer may affect patients' employment and financial health.[115] The Society of Gynecologic Oncology describes methods for assessing social needs affecting quality of life among patients with gynecologic malignancies, including financial, psychological, and spiritual needs; issues with job, transportation, food, housing, and utility insecurities; and caregiver burden.[117]

Premenopausal patients who undergo BSO during their course of treatment will usually experience an abrupt surgical menopause, and the associated vasomotor symptoms can contribute to physical discomfort.[118] In a statement endorsed by the North American Menopause Society, the Society of Gynecologic Oncology states that estrogen therapy can be prescribed for most women with epithelial ovarian cancer. Hormone therapy is not recommended for patients with low-grade serous and endometrioid ovarian cancers because those cancers may respond to treatment with antiestrogen therapies. The Society of Gynecologic Oncology states that there are insufficient data to make a recommendation for HT in women with a history of borderline tumors of the ovary.[119] For patients at high risk who elect risk-reducing salpingo-oophorectomy before menopause and who do not have a personal history of hormone-sensitive breast cancer precluding HT use, the decision to use HT should be individualized and account for the effects of early menopause on long-term health and wellness, in addition to any increased risk for breast cancer.[112]

For women who are awaiting treatment or for those who undergo fertility-sparing surgery, the Centers for Disease Control and Prevention's Medical Eligibility Criteria for Contraceptive Use considers all contraceptives to be category 1 in the setting of ovarian cancer, meaning that there is no restriction for the use of the contraceptive method[120] (Appendix 8, http://links.lww.com/AOG/D170, provides a complete evidence summary.)

RESEARCH GAPS AND OPPORTUNITIES

The evidence review and stakeholder discussion identified many research gaps and opportunities for ovarian cancer, the highest priority of which are listed here (Appendices 2–8, http://links.lww.com/AOG/D170, provide a more thorough analysis of research gaps and opportunities for each topic).Understand the epidemiology of and risk factors for ovarian cancer in the transgender communityConduct intervention trials of preventive measures in women at high or average riskObtain prospective data on opportunistic salpingectomy at the time of bilateral tubal sterilization or other pelvic surgeryCollect data on salpingectomy with delayed oophorectomy in patients with *BRCA1* and *BRCA2* mutationsDevelop effective screening or early diagnosis strategies for patients at average and high riskRefine risk stratification in patients at high riskOptimize methods to evaluate and manage adnexal masses that are found incidentallyOptimize ovarian cancer screening for individuals at high risk who choose to delay or forego risk-reducing salpingo-oophorectomyRefine and standardize criteria for patient referralEducate health care practitioners about which patients would benefit from subspecialty referralDevelop best practices to mitigate ovarian cancer treatment-related changes in sexualityImprove the understanding of stigma after hysterectomy for ovarian cancer and develop best practices to enhance body-positive treatment

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